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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
10 080,980	FEDER ET AL.
Examiner	**Art Unit**
Daniel M Sullivan	1636

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11*
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

This Office Action is a response to the "Reply under 37 C.F.R. §1.111" filed 18 March 2003 (Paper No. 13) in response to the Non-Final Office Action mailed 18 November 2002 (Paper No. 10). Claims 20-41 are pending and under consideration herein.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 20 and 30-41 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to the rejection of record, Applicant argues that the specification as filed discloses an extensive list of representative species and relevant characteristics of the species. Applicant specifically identifies teachings of N-terminal and C-terminal deletion polypeptides and nucleic acid sequences encoding them and the use of conservative substitutions in generating variants of the polynucleotides and polypeptides. Applicant asserts that the description of the features of SEQ ID NO: 1 and 2 constitutes a recitation of the relevant identifying characteristics common to the members of the genus because the members included within the genus will be encoded by a variant of SEQ ID NO: 1 and will share features of the reference sequence. That is, the identifying characteristics of the members of the genus are those of the reference sequence. Applicant argues, "in view of (a) the extensive disclosure of N- and C-terminal deletion polypeptides...(b) the disclosure of species comprising conservative substitutions of SEQ ID

NO: 2, (c) the recitation of identifying characteristics of the members of the claimed genus, and (d) the high level of skill in the art" the claims meet the written description requirement of 35 U.S.C. §112, first paragraph.

This argument has been fully considered but is not found persuasive because it ignores the basis for the rejection which is, "[t]he ability of a DNA molecule to hybridized to another molecule or 70% identity is not a relevant identifying characteristic because the ability to hybridize or 70% identity at the nucleic acid level cannot be reliably correlated with the true function of the molecule" (Paper No. 5, page 5, first paragraph). Applicant seems to be arguing that the mere sequence of nucleotides or amino acids that make up a nucleic acid or protein is the relevant identifying characteristic of the molecule. However, the primary structure of a nucleic acid or polypeptide is a relevant identifying characteristic only insofar as that structure can be correlated with a function. The skilled artisan would understand that it is the function of a nucleic acid or protein that is the relevant identifying characteristic of the molecule because it is the function, not the structure, which has utility. Clearly a recitation of primary structure does not provide the relevant identifying characteristics of the claimed molecules because the vast majority of the molecules that meet the structural limitation would not have the same function as the nucleic acid set forth as SEQ ID NO: 1 or the polypeptide set forth as SEQ ID NO: 2. If the instant disclosure had described the nucleic acids or polypeptides such that the skilled artisan could distinguish, or envision molecules encompassed by the structural limitations of the claims having a defined function from those molecules that are non-functional, the written description requirement would be satisfied. In contrast, the instant disclosure provides a description of structure with no correlation at all of structure with function. Although the specification provides

a general teaching of amino acid substitutions considered in the art to be conservative, one of ordinary skill in the art understands that the effect of amino acid substitution at any given position in a polypeptide on the function of that polypeptide is unpredictable. Therefore, even if the claims were limited to polypeptides comprising only conservative amino acid substitutions, which they are not, the claimed subject matter would still comprise many molecules that would not have the function of the polypeptide set forth as SEQ ID NO: 2. As the teachings of the specification provide no means by which the skilled artisan could envision those polypeptides encompassed within the claimed genus that have a defined function, clearly the disclosure fails to teach the relevant identifying characteristics of said genus. Thus, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope and the claims stand rejected.

Claims 20-41 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention.

In response to the rejection of record, Applicant asserts that the claims are enabled by "the disclosures of the present U.S. patent application, coupled with information known in the art, without undue experimentation" (Paper No. 13, page 6). Applicant argues that the Patent Office has not provided any concrete evidence that one of ordinary skill in the art would not be enabled by the disclosure and relevant art to employ the compositions and methods of the present disclosure. Applicant argues that the rejection is improperly requiring that Applicant submit working examples in order to comply with the enablement requirement.

These arguments have been fully considered but are not found persuasive. The previous office action cites several teachings from the relevant art indicating that the function of the polypeptide encoded by the claimed nucleic acids cannot be predicted from the teachings of the disclosure. In particular, the only protein having empirically demonstrated function identified as homologous with the instant disclosed polypeptide is the MaxiK βsubunit. Jiang *et al.* teaches that polypeptides having the function of MaxiK βsubunits have 71% identity across several mammalian species (page 8). In contrast, the polypeptide set forth as SEQ ID NO: 2 has 0% identity with the MaxiK βsubunit. Further, the Office Action cites teachings from the TrEMBL database demonstrating that the function of the polypeptides to which the instant SEQ ID NO: 2 is most similar was unknown at the time the application was filed. As stated in the previous office action, "the skilled artisan would not predict that a mammalian protein having no identity to the MaxiK channel β-subunit would have the same, or even a closely related function. In the case of predicting the function of a polypeptide based on similarity to proteins having unknown function, even if, for the sake of argument, the skilled artisan could predict with a high degree of certainty that the structurally related proteins had the same function, the function of the proteins remains unknown" (page 8).

The courts have held that sound scientific reasoning is "an acceptable alternative to patents and printed publications in support of an examiner's holding that a disclosure is not enabling" (*Ex parte Sudilovsy*, 21 USPQ2d 1702 (BPAI 1991)). In the instant case, the Examiner is merely reasoning that, because the polypeptide encoded by the claimed nucleic acid is most similar to proteins of unknown function, the function of the polypeptide encoded by the said claimed polynucleotide must also be unknown. Clearly, this is sound scientific reasoning.

With regard to the absence of working examples, Applicant correctly points out that a disclosure need not contain working examples to comply with the enablement standard. However, the section of the MPEP cited by Applicant (i.e., §2164.02) goes on to state, "[w]hen considering the factors relating to a determination of non-enablement, if all other factors point to enablement, then the absence of working examples will not by itself render the invention non-enabled" (emphasis added). For reasons provided in the previous Office Action and herein, the skilled artisan would not know the function of the claimed nucleic acid, or polypeptide encoded thereby, and thus would not know how to use the claimed invention. Because these factors point to non-enablement, the absence of a single working example is clearly a relevant factor to be considered in determining the enablement of the claims.

Applicant next argues that the specification provides guidance for cloning the polynucleotides of the present invention, expressing the polypeptides of the present invention, performing bioinformatic analyses, identifying the presence of an abnormal level of a polypeptide of the present invention, and tissue profiling among other examples. Applicant asserts that these teachings coupled with standard molecular and or biochemical laboratory techniques would be fully enabling for the claimed subject matter. However, Applicant is reminded that the instant rejection is based on the absence of teachings that would enable the skilled artisan to use the claimed invention. The basic assertion of the previous Office Action is that the function of the claimed invention is unknown, and this assertion is not challenged by Applicant. In the absence of a known function for the claimed invention, the teachings of the specification and prior art serve only as a means to determine the function of said invention so that the skilled artisan can then devise a use for the invention. Applicant is reminded, "[l]aw

requires that disclosure in application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use for themselves" (*In re Gardner, Roe and Willey* 166 USPQ 138).

Next, Applicant acknowledges that some experimentation might be required in order to develop the diagnostics or therapeutics which are set forth as utilities for the claimed invention, but that, "[b]y following the guidance provided in the present disclosure, one or [sic] ordinary skill in the art would be able to develop a diagnostic protocol and or therapeutics" without engaging in experimentation beyond what would be considered routine in the art. This argument is not found persuasive because the disclosure does not provide the most essential guidance to developing a diagnostic protocol and or therapeutic, which is the function of the claimed invention. Without knowing the function of the polypeptide encoded by the claimed polynucleotide, the skilled artisan is directionless and left to conducting blind trial and error experimentation to divine a use for the claimed invention. In *In re Wands*, the court states, "[t]he determination of what constitutes undue experimentation in a given case requires the application of standard reasonableness, having due regard for the nature of the invention and the state of the art" (at 1404). As stated in the previous Office Action, "Applicant has placed on the shoulders of the skilled artisan seeking to use the claimed polynucleotides the burden of: first, identifying the activity of the polynucleotides or encoded polypeptides; next, correlating that activity with a disease state; and finally, developing diagnostics or therapeutics from the claimed polypeptides" (page 7). Clearly, the burden of experimentation placed by Applicant on one of ordinary skill seeking to use the claimed invention is not reasonable.

Applicant argues that the claimed polynucleotides and or polypeptides of the present invention have uses other than as a therapeutic or diagnostic which are presented in the specification. Applicant cites Example 19 and pages 71-101 of the specification, which describes antibody formation and guidance on pages 101-113 regarding using antibodies in immunophenotyping, assays of antibody binding, therapy and antibody based gene-therapy. Applicant points to: Example 23, which presents a method of determining alterations in a gene corresponding to a polynucleotide; Example 24, which describes a method of detecting abnormal levels of a polypeptide in a biological sample; and Example 31, which describes a method of generating a transgenic animal. This argument is not persuasive because, in the absence of a teaching of function or some correlation to human disease, the antibodies and methods have no use other than to identify a patentable utility for the claimed invention. Applicant asserts that antibodies raised against the polypeptide can be used in immunophenotyping or assays of antibody binding, but does not indicate what the skilled artisan is to do with the phenotyping or binding data obtained. Applicant cites raising antibodies as an alternative to therapeutic or diagnostic utility, but then states that the antibodies are to be used for therapeutic or diagnostic applications. Likewise, Applicant has provided no use for applications such as determining alterations in a gene corresponding to a polynucleotide, detecting abnormal levels of a polypeptide or generating a transgenic animal other than to investigate the function of the claimed invention itself, or as a therapeutic or diagnostic. Therefore, in the absence of a known function for the claimed invention, the disclosure does not provide a patentable utility other than as a diagnostic or therapeutic. For reasons of record, the skilled artisan would not be able to use the claimed invention for that purpose without first engaging in undue experimentation.

In support of claim 34, directed to a method of diagnosing a pathological condition or susceptibility to a pathological condition, Applicant points to a general teaching of a standard diagnostic assay, at pages 180 and 182 of the specification, and Example 6, and asserts that the claimed method could be used to diagnose a condition associated with the NF-κB pathway. Example 6 provides data from RNAi experiments with E4-1 cells which applicant characterizes as indicating that *Drosophila* protein CG10465 serves as a positive regulator in an innate immunity similar to IκKB. Applicant seems to be asserting that these findings indicate that the claimed method likely has utility for diagnosis of inflammatory diseases including rheumatoid arthritis, asthma, multiple sclerosis and osteoarthritis. This argument is not persuasive because, as pointed out in the previous office action, the "functional data obtained using RNAi must be extrapolated not only from a polynucleotide encoding a protein having only 24% identity, but also from data obtained in insect cells to the mammalian organism" (bridging pages 9 and 10). Furthermore, even if one were to assume, *arguendo*, that the data provided is enabling for a method of diagnosing an inflammatory disease, the claim is not so limited. Applicant is claiming a method of diagnosing any disease that might be associated with a mutation in the disclosed polynucleotide. Clearly the teachings of Example 6 do not support such breadth.

Finally, Applicant points to the recitation of use of CLUSTALW sequence alignment in claim 38 and teachings in the specification related to CLUSTALW sequence alignment as more guidance with which to practice the claimed invention. However, this teaching is not enabling because, like the methods of raising antibodies and determining alterations in a gene addressed above, the guidance provided serves only to investigate the claimed invention and thus does not constitute a patentable utility for said invention.

Thus, for the reasons of record in Paper No. 10 and herein above, the claims stand rejected.

Claim Rejections - 35 USC § 102

The Examiner appreciates Applicant's identifying typographical errors in the Office Action and correctly assuming that the art referred to in the Office Action is NCBI ENTREZ ACCESSION NO: gi:10039473 and gi:2133864.

Claims 20, 25, 28-30 and 38 stand rejected under 35 U.S.C. 102(a) as being anticipated by NCBI ENTREZ ACCESSION NO: gi:10039473 available as of September 8, 2000 as evidenced by the notation in the first line of "COMMENT".

In response to the rejection of record, Applicant argues that the claims are not anticipated by gi:10039473 because the first 12 amino acids of SEQ ID NO: 2 are not disclosed therein. This argument has been fully considered but is not found persuasive because the art is cited only against claims directed to polynucleotides that are not limited to encoding the full length SEQ ID NO: 2. Claims 20(e) and 25 are directed to a polynucleotide encoding amino acids 34-134 of SEQ ID NO: 2; claims 20(e) and 28 are directed to a polynucleotide encoding at least 50 contiguous amino acids of SEQ ID NO: 2; claim 20(f) and 29 are directed to a polynucleotide which represents a complementary sequence of 20(e) or (e); and 20(g) and 30 are directed to a polynucleotide capable of hybridizing with any of the polynucleotides of 20(a)-(f).

Next, Applicant argues that because gi:10039473 is an annotated chromosomal sequence it is excluded from the claimed subject matter by teachings in the specification which state, "[t]he term "isolated" does not refer to genomic or cDNA libraries, whole cell or mRNA

preparations, genomic DNA preparations (including separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide sequences of the present invention" (Paper No. 13, page 11; emphasis added). Applicant argues that this teaching explicitly excludes genomic DNA from the scope of the instant claims. This argument is not found persuasive because it mischaracterizes the cited teaching from the specification. The teaching actually excludes complex mixtures of DNA which do not demonstrate the distinguishing features of the polynucleotide sequence claimed. The teaching does not exclude all genomic DNA from the claimed subject matter. gi:10039473 sets forth the actual sequence of the claimed polynucleotide and thus clearly demonstrates a distinguishing feature of the present invention. Furthermore, possession of an "isolated" nucleic acid according to the teachings of the specification is inherent in the disclosure of a polynucleotide sequence because sequence information cannot be obtained from a complex mixture of DNA.

Thus for reasons of record and set forth herein, the claims stand rejected under 35 U.S.C. §102(a) as anticipated by gi:10039473.

Claims 20-26, 28-30 and 38 stand rejected under 35 U.S.C. 102(b) as being anticipated by NCBI ENTREZ ACCESSION NO: gi:2133864.

In response to the rejection of record, Applicant again argues that the claims are not anticipated by the art because the art discloses the sequence of a genomic DNA. For the reasons set forth above, this argument is not deemed persuasive. To summarize, the teaching cited by applicant actually excludes complex mixtures of DNA and not all genomic DNA. The teaching

does not exclude all genomic DNA from the claimed subject matter. gi:2133864 sets forth the actual sequence of the claimed polynucleotide and thus clearly demonstrates a distinguishing feature of the present invention. Furthermore, possession of an "isolated" nucleic acid according to the teachings of the specification is inherent in the disclosure of a polynucleotide sequence because sequence information cannot be obtained from a complex mixture of DNA.

Thus for reasons of record and set forth herein, the claims stand rejected under 35 U.S.C. §102(a) as anticipated by gi:2133864.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
May 22, 2003

JAMES KETTER
PRIMARY EXAMINER